

AMENDMENTS TO THE SPECIFICATION

Please substitute the below paragraph for the paragraph beginning on page 2, line 16 and ending on page 3, line 5.

Conveniently, the oligodeoxynucleotide to connexin 43 is selected from:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC (SEQ ID NO:1);
GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (SEQ ID NO:2); and
GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT (SEQ ID NO:3)

Most conveniently, the oligodeoxynucleotide to connexin 43 is:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC (SEQ ID NO:1).

Conveniently, the oligodeoxynucleotide to connexin 26 is:

TCC TGA GCA ATA CCT AAC GAA CAA ATA (SEQ ID NO:4).

Conveniently, the oligodeoxynucleotide to connexin 31.1 is:

CGT CCG AGC CCA GAA AGA TGA GGT C (SEQ ID NO:5).

Conveniently, the oligodeoxynucleotide to connexin 32 is:

TTT CTT TTC TAT GTG CTG TTG GTG A (SEQ ID NO:6).

The anti-sense polynucleotides may be formulated for parenteral, intramuscular, intracerebral, intravenous, subcutaneous or transdermal administration. The antisense polynucleotides are preferably administered topically (at the site to be treated). Suitably the antisense polynucleotides are combined with a pharmaceutically acceptable carrier, vehicle or diluent to provide a pharmaceutical composition.

Please substitute the below paragraph for the paragraph beginning on page 11, line 9 and ending on page 11, line 25.

The precise sequence of the antisense polynucleotide used in the invention will depend upon the target connexin protein. For connexin 43, the applicant's have found ODN's having the following sequences to be particularly suitable:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC (SEQ ID NO:1);
GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (SEQ ID NO:2); and
GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT (SEQ ID NO:3)

ODN's directed to other connexin proteins can be selected in terms of their nucleotide sequence by any convenient, and conventional, approach. For example, the computer programmes MacVector and OligoTech (from Oligos etc. Eugene, Oregon, USA) can be used. For example, ODN's for connexins 26, 31.1 and 32 have the following sequences:

5' TCC TGA GCA ATA CCT AAC GAA CAA ATA (connexin 26) (SEQ ID NO:4)

5' CGT CCG AGC CCA GAA AGA TGA GGT C (connexin 31.1) (SEQ ID NO:5)

5' TTT CTT TTC TAT GTG CTG TTG GTG A (connexin 32) (SEQ ID NO:6)

Please substitute the below paragraph for the paragraph starting on page 14, line 4 and ending on page 14, line 21.

Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighbourhood word score threshold (Altschul *et al*, supra). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either

sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) *Proc. Natl. Acad. Sci. USA* 89: 10915-10919) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

Please substitute the below paragraph for the paragraph beginning on page 17, line 5, and ending on page 17, line 12.

Antisense oligodeoxynucleotides to Connexin 43

DB1 GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (SEQ ID NO:2)

CG1 GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT (SEQ ID NO:3)

Control oligodeoxynucleotides

DB1(sense) GAC AGA AAC AAT TCC TCC TGC CGC AAT TAC (SEQ ID NO:7)

DB1(chick) GTA GTT ACG ACA GGA GGA ATT GTT CTC GTC (SEQ ID NO:8)

CV3(random) TCG AAC TGT CAA GAC TGC TAT GGC GAT CAT (SEQ ID NO:9)

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Please substitute the below paragraph for the paragraph beginning on page 20, line 2 and ending on page 20, line 5.

Oligodeoxynucleotides were prepared with the following sequences:

GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (connexin 43) (SEQ ID NO:2)

TTG TGA TTT ATT TAG TTC GTC TGA TTT C (random control) (SEQ ID NO:10)

Please substitute the below paragraph for the paragraph beginning on page 27, line 4 and ending on page 27, line 7.

Oligodeoxynucleotides were prepared with the following sequences:

GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (connexin 43) (SEQ ID NO:2)

GAC AGA AAC AAT TCC TCC TGC CGC AAT TAC (sense control) (SEQ ID NO:7)

Please substitute the below paragraph for the paragraph beginning on page 29, line 11 and ending on page 29, line 13.

Oligodeoxynucleotides were prepared with the following sequences:

GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (connexin 43) (SEQ ID NO:2)

GAC AGA AAC AAT TCC TCC TGC CGC AAT TAC (sense control) (SEQ ID NO:7)

Please substitute the below paragraph for the paragraph beginning on page 33, line 5 and ending on page 33, line 8.

Oligodeoxynucleotides were prepared with the following sequences:

GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC (connexin 43) (SEQ ID NO:2)

GAC AGA AAC AAT TCC TCC TGC CGC AAT TAC (sense control) (SEQ ID NO:7)

Please substitute the below paragraph for the paragraph beginning on page 34, line 16 and ending on page 34, line 36.

Table 1 (SEQ ID NO:12)

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1 atgggtgact ggagcgccctt aggcaaacctc cttgacaagg ttcaagccta ctcaactgct
61 ggaggggaagg tgtggctgtc agtacttttc atttccgaa tctgtctgct ggggacagcg
121 gttgagtcag cctggggaga tgagcagtct gcccttcgtt gtaacactca gcaacctggt
181 tgtgaaaatg tctgctatga caagtcttcc ccaatctctc atgtgcgctt ctgggtctctg
241 cagatcatat ttgtgtctgt acccacactc ttgtacctgg ctcatgtgtt ctatgtgatg
301 cgaaaggaag agaaactgaa caagaaagag gaagaactca aggttgccca aactgatggt
361 gtcaatgtgg acatgcactt gaagcagatt gagataaaga agttcaagta cggtattgaa
421 gagcatggtg aggtgaaaat gcgagggggg ttgctgcgaa cctacatcat cagtatcctc
481 ttcaagtcta tctttgaggt ggccttcttg ctgaccagt ggtacatcta tggattcagc
541 ttgagtctg tttacacttg caaaagagat cctgcccac atcaggtgga ctgttctctc
601 tctgcccga cggagaaaac catcttcac atcttcatgc tgggtggtgc cttggtgtcc
661 ctggccttga atalcattga actcttctat gttttcttca agggcgtaa ggatcgggtt
721 aagggaaga gcgaccctta ccatgcgacc agtgggtgcg tgagccctgc caaagactgt
781 ggggtcctaaa aatatgctta ttcaatggc tgctctcac caaccgtcc cctctgcct
841 atgtctctc ctgggtacaa gctgggtact ggcgacagaa acaattctc ttgccgaat
901 tacaacaagc aagcaagtga gcaaaactgg gctaattaca gtgcagaaca aaatcgaatg
961 gggcagggcg gaagcaccat ctctaactcc catgcacagc cttttgattt ccccgatgat
1021 aaccagaatt ctaaaaaact agctgctgga catgaattac agccactagc cattgtggac
1081 cagcgacctt caagcagagc cagcagctgt gccagcagca gacctcgcc tgatgacctg
1141 gagatctag
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